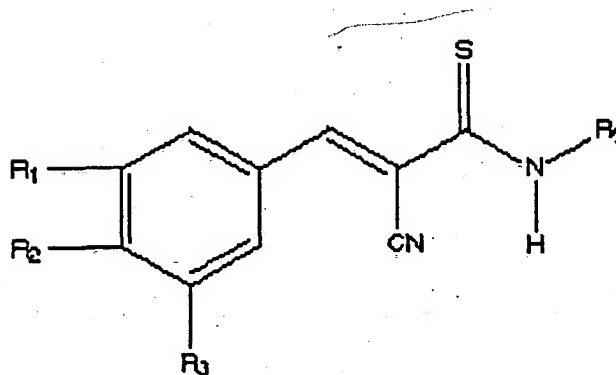


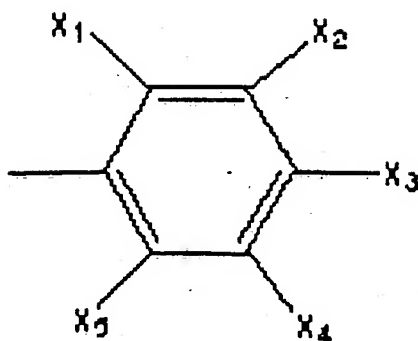
CLAIMS

1. A protein kinase inhibitor composition comprising a compound having the chemical formula:



wherein R<sub>1</sub>, R<sub>2</sub>, and R<sub>3</sub> is each independently selected  
5 from the group consisting of alkyl, alkenyl, alkynyl, alkoxy, alkylaryl, OH, amine, thioether, SH, halogen, hydrogen, NO<sub>2</sub> and NH<sub>2</sub>; and R<sub>4</sub> is an alkylaryl comprising an

alkyl group and an aryl group having the following structure:



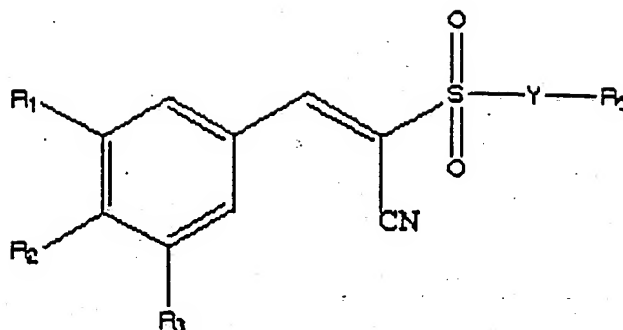
wherein X<sub>1</sub>, X<sub>2</sub>, X<sub>3</sub>, X<sub>4</sub>, and X<sub>5</sub> is each independently selected from the group consisting of hydrogen, halogen, alkyl, trihalomethyl, and NO<sub>2</sub>.

2. The composition of claim 1, wherein said R<sub>1</sub> and said R<sub>2</sub> is OH, and said R<sub>3</sub> is hydrogen, and said compound significantly inhibits HER-2 activity.

3. The composition of claim 2, further comprising a physiologically acceptable carrier.

4. The composition of claim 1, wherein said compound is M13.

5. A HER-2 protein kinase inhibitor composition comprising a compound having the chemical formula:



wherein  $R_1$ ,  $R_2$ , and  $R_3$  is each independently selected from the group consisting of alkyl, alkenyl, alkynyl, alkoxy, alkylaryl, OH, amine, thioether, SH, halogen, hydrogen,  $\text{NO}_2$ , and  $\text{NH}_2$ ;

5     Y is either nothing,  $-\text{C}(\text{CN})=\text{C}-$ , -alkyl- or -NH-alkyl-; and

$R_4$  is either CN or aryl.

6. The composition of claim 7, wherein said aryl phenyl or pyridyl.

10     7. The composition of claim 6, wherein said aryl contains 1 to 5 substitutents independently selected from the group consisting of: alkyl and OH; and the remaining substituents are hydrogen.

8. The composition of claim 9, wherein said alkyl is  
15 either methyl, t-butyl or isopropyl.

9. The composition of claim 9, wherein 1-3 of said substituents is selected from the group consisting of OH, methyl, t-butyl or isopropyl.

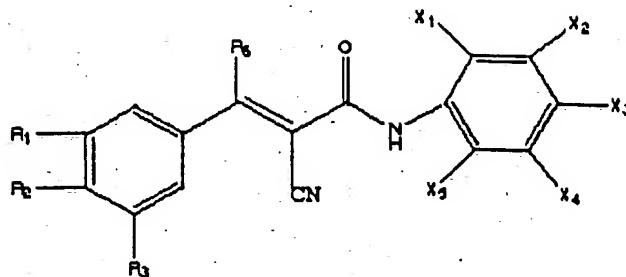
10. The composition of claim 5, wherein said R<sub>1</sub> is t-  
5 butyl or isopropyl;  
said R<sub>2</sub> is OH;  
said R<sub>3</sub> is t-butyl or isopropyl;  
said Y is either CH<sub>2</sub>, or C(CN)=C; and  
said R<sub>4</sub> is either CN, phenyl or pyridyl.

10 11. The composition of claim 5, wherein said R<sub>1</sub> is t-  
butyl or isopropyl;  
said R<sub>2</sub> is OH;  
said R<sub>3</sub> is t-butyl or isopropyl;  
said Y is either nothing or a lower alkyl; and  
15 said R<sub>4</sub> aryl is either phenyl or pyridyl.

12. The composition of claim 5, wherein said R<sub>1</sub> is t-  
butyl or isopropyl;  
said R<sub>2</sub> is OH;  
said R<sub>3</sub> is t-butyl or isopropyl;  
20 said Y is -NH-lower alkyl-; and  
said R<sub>4</sub> aryl is either phenyl or pyridyl.

13. The composition of claim 5, wherein said compound is selected from the group consisting of: M26, M27, M29, M30, M32, M33, M34, M37, M40, M41, M42, M43, M44 and M45.

14. A protein kinase inhibitor composition comprising a compound having the chemical formula:



wherein  $R_1$ ,  $R_2$ ,  $R_3$ , and  $R_4$  is each independently  
5 selected from the group consisting of alkyl, alkenyl, alkynyl, alkoxy, alkylaryl, halogen, hydrogen, OH, amine, thioether, SH and  $NH_2$ ; and

$X_1$ ,  $X_2$ ,  $X_3$ ,  $X_4$ , and  $X_5$  are each independently selected  
from the group consisting of hydrogen, halogen, trihalo-  
10 methyl, alkyl, alkenyl, alkynyl, alkoxy, and  $NO_2$ , provided  
that at least one of  $X_1$ ,  $X_2$ ,  $X_3$ ,  $X_4$ , and  $X_5$  is a trihalomethyl.

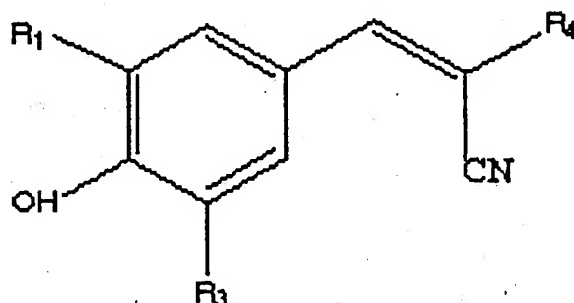
15. The composition of claim 14, wherein said  $R_1$  is  
OH, said  $R_2$  is OH, said  $R_3$  is hydrogen,  $R_4$  is hydrogen, and  
15 four of said  $X_1$ ,  $X_2$ ,  $X_3$ ,  $X_4$ , and  $X_5$  is hydrogen.

16. The composition of claim 15, wherein said  
compound inhibit HER-2 activity.

17. The composition of claim 15, further comprising a physiologically acceptable carrier.

18. The composition of claim 15, wherein said compound is M15.

5 19. A protein kinase inhibitor composition comprising a compound having the chemical formula:



wherein R<sub>1</sub> and R<sub>3</sub> is each independently selected from the group consisting of alkyl, alkenyl, alkynyl, alkoxy, alkylaryl; and

10 R<sub>4</sub> is selected from the group consisting of alkyl, alkylaryl, thioamide, and amide.

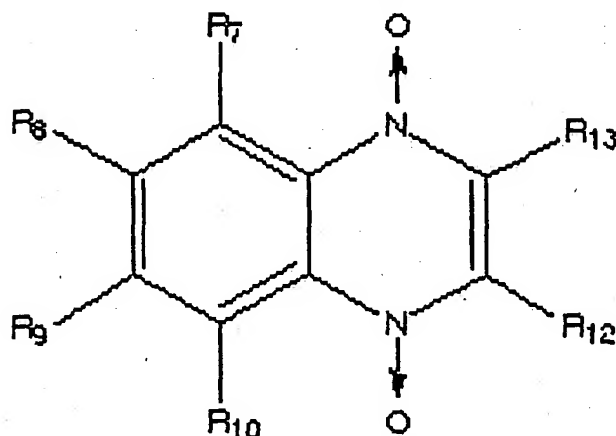
20. The composition of claim 19, wherein R<sub>1</sub> and R<sub>3</sub> is each independently an alkyl.

21. The composition of claim 20, wherein said  
15 compound inhibits HER-2 activity.

22. The composition of claim 21, further comprising a physiologically acceptable carrier.

23. The composition of claim 19, wherein said compound is M19, M11, M18, and M17.

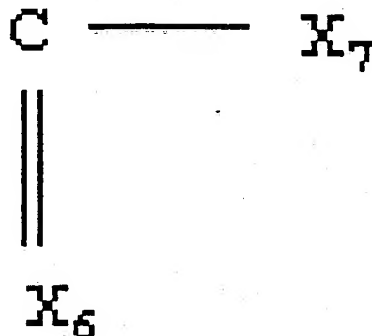
5 24. A protein kinase inhibitor composition comprising a compound having the chemical formula:



wherein R<sub>7</sub>, R<sub>8</sub>, R<sub>9</sub>, and R<sub>10</sub>, is each independently selected from the group consisting of alkyl, alkenyl,

alkynyl, alkoxy, alkylaryl, OH, NO<sub>2</sub>, amine, thioether, SH, halogen, hydrogen and NH<sub>2</sub>;

R<sub>12</sub> has the chemical structure:



wherein X<sub>6</sub> is either O or S and X<sub>7</sub> is either methyl or trihalomethyl; and

R<sub>13</sub> is either aryl or alkylaryl.

25. The composition of claim 24, wherein said R<sub>7</sub>, R<sub>8</sub>, R<sub>9</sub>, and R<sub>10</sub>, are hydrogen; and said R<sub>13</sub> is aryl.

26. The composition of claim 25, wherein said compound inhibits HER-2 activity.

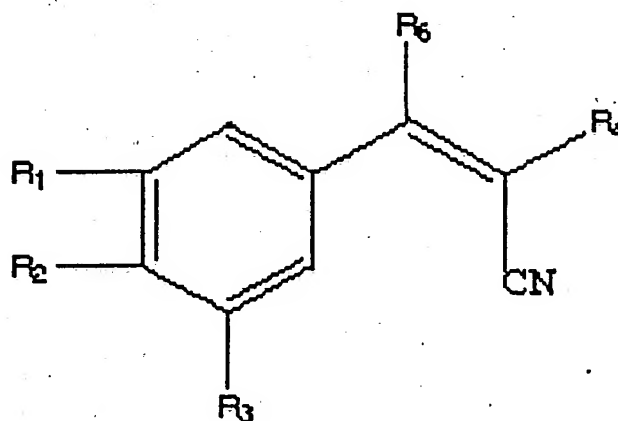
27. The composition of claim 24, further comprising a physiologically acceptable carrier.



28. The composition of claim 24, wherein said compound is either N10 or N12.

29. A protein kinase inhibitor composition comprising a compound selected from the group consisting of: M16,  
5 N17, N21, N22, N23, N29, R10, R11, and R12.

30. A method of treating a patient having a cell proliferative disorder comprising the step of administering to said patient a therapeutical effective amount of a compound having the chemical formula:

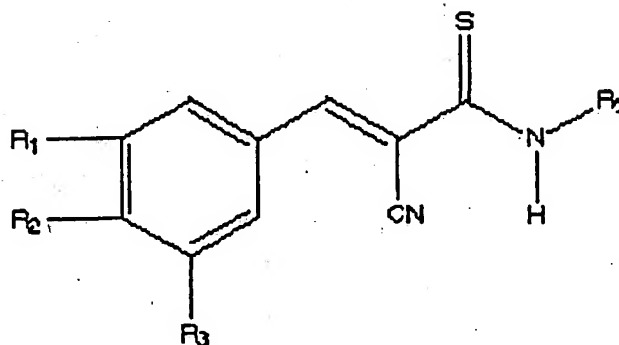


10 wherein R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, and R<sub>4</sub> is each independently selected from the group consisting of alkyl, alkenyl, alkynyl, alkoxy, alkylaryl, OH, NO<sub>2</sub>, amine, thioether, SH, halogen, hydrogen and NH<sub>2</sub>; and

$R_4$  is selected from the group consisting of alkyl, alkylaryl, thioamide, amide, CN and sulfonyl.

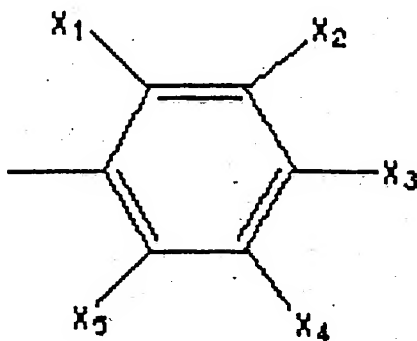
31. The method of claim 30, wherein said disorder is characterized by abnormal or overactivity of HER-2.

5        32. The method of claim 30 wherein said compound has the chemical formula:



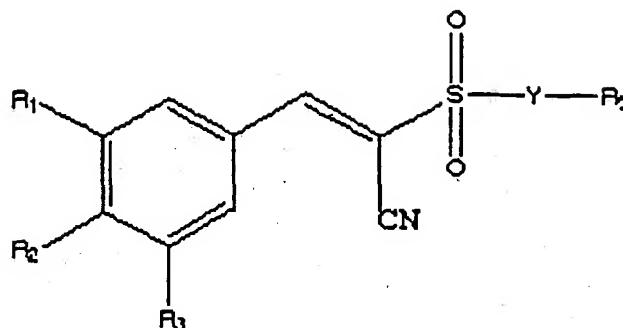
wherein  $R_1$ ,  $R_2$ , and  $R_3$  is each independently selected from the group consisting of alkyl, alkenyl, alkynyl, alkoxy, alkylaryl, OH, amine, thioether, SH, halogen,  
10 hydrogen,  $\text{NO}_2$  and  $\text{NH}_2$ ; and

R<sub>5</sub> is an alkylaryl comprising an alkyl group and an aryl group having the following structure:



wherein X<sub>1</sub>, X<sub>2</sub>, X<sub>3</sub>, X<sub>4</sub>, and X<sub>5</sub> is each independently selected from the group consisting of hydrogen, halogen, alkyl, trihalomethyl, and NO<sub>2</sub>.

33. The method of claim 32, wherein said compound has the chemical formula:

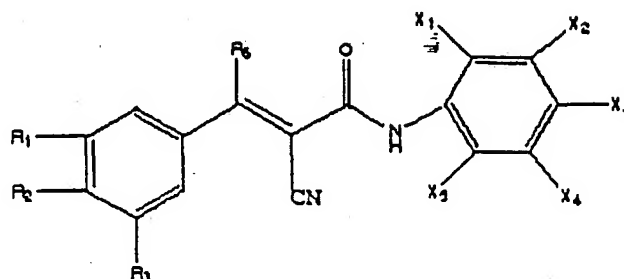


wherein  $R_1$ ,  $R_2$ , and  $R_3$  is each independently selected from the group consisting of alkyl, alkenyl, alkynyl, 5 alkoxy, alkylaryl, OH, amine, thioether, SH, halogen, hydrogen,  $\text{NO}_2$  and  $\text{NH}_2$ ;

$Y$  is either  $\text{C}(\text{CN})=\text{C}$  or alkyl; and

$R_5$  is either CN or aryl.

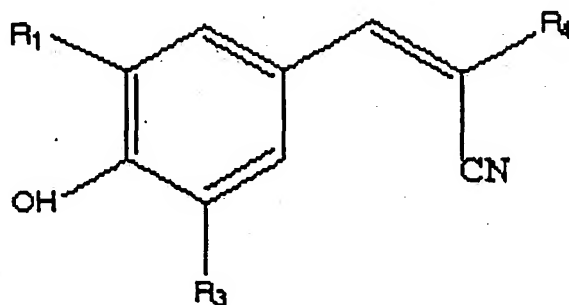
34. The method of claim 30, wherein said compound has 10 the chemical formula:



wherein  $R_1$ ,  $R_2$ ,  $R_3$ , and  $R_4$  is each independently selected from the group consisting of alkyl, alkenyl, alkynyl, alkoxy, alkylaryl, halogen, hydrogen, OH, amine, thioether, SH and  $NH_2$ ; and

$X_1$ ,  $X_2$ ,  $X_3$ ,  $X_4$ , and  $X_5$  are each independently selected from the group consisting of hydrogen, halogen, trihalomethyl, alkyl, alkenyl, alkynyl, alkoxy, and  $NO_2$ , provided that at least one of  $X_1$ ,  $X_2$ ,  $X_3$ ,  $X_4$ , and  $X_5$  is a trihalomethyl.

35. The method of claim 30, wherein said compound has the chemical formula:



wherein  $R_1$  and  $R_3$  is each independently selected from the group consisting of alkyl, alkenyl, alkynyl, alkoxy, alkylaryl; and

R<sub>4</sub> is selected from the group consisting of alkyl, alkylaryl, thioamide, and amide.

36. The method of claim 30, wherein said disorder is characterized by inappropriate activity of EGF-R.

5        37. The method of claim 31, wherein said cell proliferative disorder is a cancer.

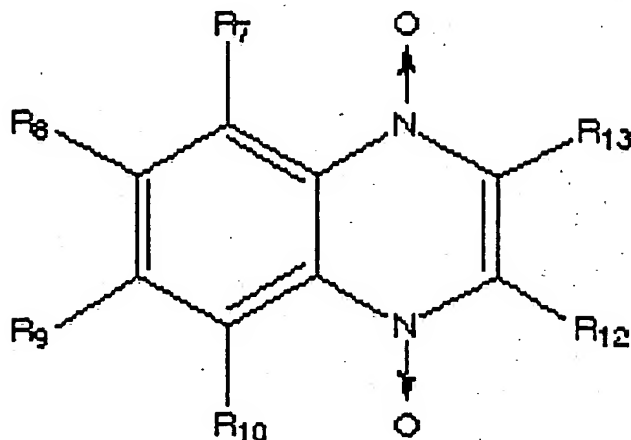
38. The method of claim 37, wherein said cancer is selected from the group consisting of breast carcinomas, stomach adenocarcinomas, salivary gland adenocarcinomas, 10 endometrial cancers, ovarian adenocarcinomas, gastric cancers, colorectal cancers, and glioblastomas.

39. The method of claim 38, wherein said cancer is breast cancer.

40. A method of treating a patient having a cancer 15 characterized by over-activity of HER2 comprising the step of administering to said patient a therapeutical effective

amount of a compound selected from the group consisting of:

a) a compound having the chemical formula:

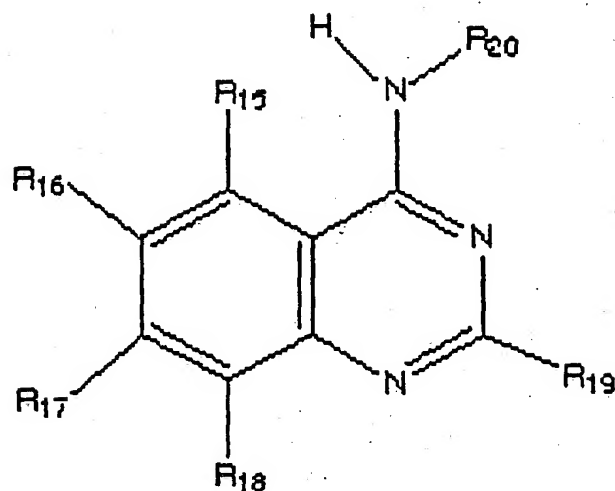


wherein R<sub>7</sub>, R<sub>8</sub>, R<sub>9</sub>, and R<sub>10</sub>, is each independently  
5 selected from the group consisting of alkyl, alkenyl, alkynyl, alkoxy, alkylaryl, OH, NO<sub>2</sub>, amine, thioether SH, halogen, hydrogen and NH<sub>2</sub>;

R<sub>12</sub> is selected from the group consisting of alkyl, alkenyl, alkynyl, alkoxy, ester, amide, thioamide,  
10 alkylaryl, trihalomethyl, CN, OH, amine, thioether SH, NH<sub>2</sub>, and hydrogen; and

R<sub>13</sub> is selected from the group consisting of aryl, alkyl, alkenyl, alkynyl, CN, alkylaryl, amide, and thioamide;

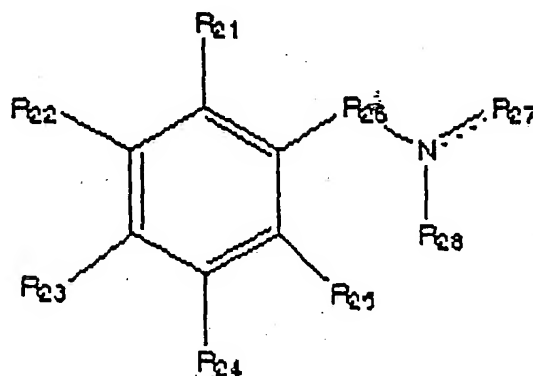
b) a compound having the chemical formula:



wherein  $R_{15}$ ,  $R_{16}$ ,  $R_{17}$ ,  $R_{18}$  and  $R_{19}$ , is each independently selected from the group consisting of hydrogen alkyl, alkenyl, alkynyl, alkoxy, OH,  $\text{NO}_2$ , amine, thioether, and  
5 SH; and

$R_{20}$  is selected from the group consisting of alkyl, aryl, and alkylaryl;

c) a compound having the chemical formula:





wherein  $R_{21}$ ,  $R_{22}$ ,  $R_{23}$ ,  $R_{24}$ , and  $R_{25}$ , are each independently selected from the group consisting of hydrogen, halogen, OH, SH, alkyl, aryl, and trihaloalkyl;

$R_{26}$  is either  $CH_2$  or  $NH$ ;

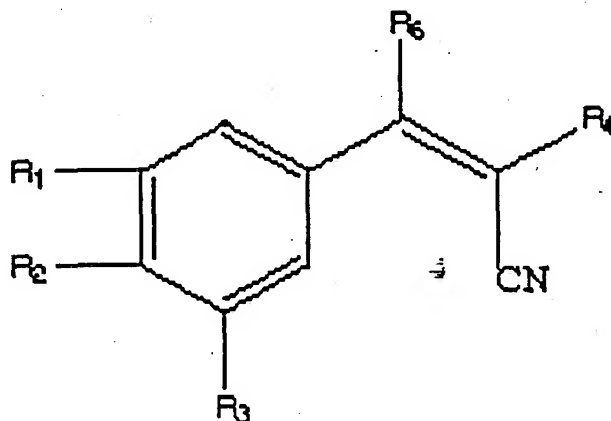
5  $R_{27}$  is either aryl or  $=C(CN)_2$ ; and

$R_{28}$  is either nothing or H, provided that if  $R_{28}$  is nothing a double bond is present between N and  $R_{27}$ ; and

d) compound  $R_9$ ,  $R_{11}$ ,  $R_{13}$ , and  $R_{15}$ .

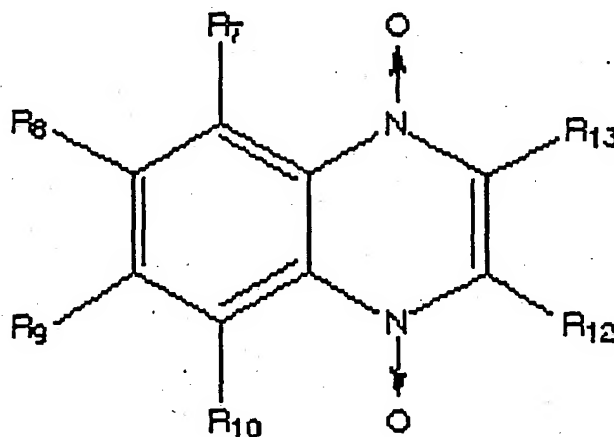
41. A method of treating a patient having a cancer  
10 characterized by inappropriate activit of EGFR comprising the step of administering to said patient a therapeutical effective amount of a compound selected from the group consisting of:

a) a compound having the chemical formula:



wherein  $R_1$ ,  $R_2$ ,  $R_3$ , and  $R_4$  is each independently selected from the group consisting of alkyl, alkenyl, alkynyl, alkoxy, alkylaryl, OH, amine, thioether, SH, halogen, hydrogen and  $NH_2$ ;  $R_4$  is selected from the group  
5 consisting of alkyl, alkylaryl, amide, thioamide, and CN;

b) a compound having the chemical formula:

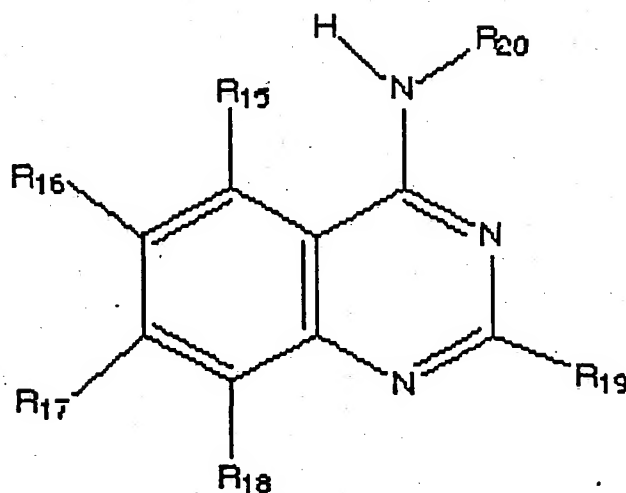


wherein  $R_7$ ,  $R_8$ ,  $R_9$ , and  $R_{10}$  is each independently selected from the group consisting of alkyl, alkenyl, alkynyl, alkoxy, alkylaryl, OH, amine, thioether, SH, halogen, hydrogen or  $NH_2$ ;  
10

$R_{12}$  is selected from the group consisting of alkyl, alkenyl, alkynyl, alkoxy, ester, amide, thioamide, alkylaryl, trihalomethyl, CN, OH, SH,  $NH_2$ , hydrogen, amine, and thioether; and

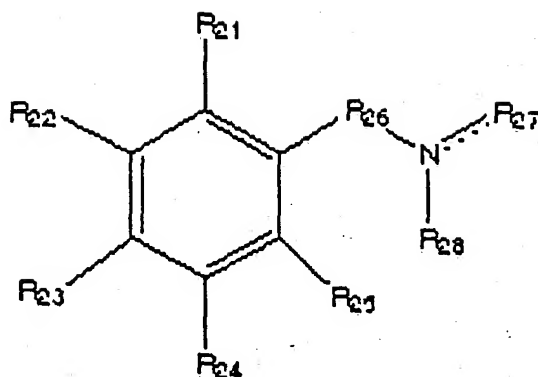
5  $R_{13}$  is selected from the group consisting of aryl, alkyl, alkenyl, alkynyl, CN, alkylaryl, thioamide, and amide;

c) a compound having the chemical formula:



10 wherein  $R_{15}$ ,  $R_{16}$ ,  $R_{17}$ ,  $R_{18}$  and  $R_{19}$ , is each independently selected from the group consisting of hydrogen alkyl, alkenyl, alkynyl, alkoxy, OH, amine, thioether and SH; and  $R_{20}$  selected from the group consisting of alkyl, aryl, or alkylaryl; and

15 d) a compound having the chemical formula:



wherein R<sub>21</sub>, R<sub>22</sub>, R<sub>23</sub>, R<sub>24</sub>, and R<sub>25</sub>, are each independently selected from the group consisting of hydrogen, halogen, OH, SH, alkyl, aryl, and trihaloalkyl;

R<sub>26</sub> is either CH<sub>2</sub> or NH;

5 R<sub>27</sub> is either aryl or =C(CN)<sub>2</sub>;

e) compound R9, R10, R11, R13, R14, and R15.

42. A method of determining whether a receptor tyrosine kinase is important for growth of a cell comprising the steps of:

- 10 a) contacting said cell with a composition comprising a compound which significantly inhibits the growth of a receptor tyrosine kinase activity selected from the group consisting of: EGF activity, PDGF activity, and HER2 activity,
- 15 b) measuring the growth of said cell after said contacting in said step (a).

43. The method of claim 42, wherein said compound significantly inhibits said activity in a growth assay.